EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Jeanne Brashear and David Gasson April 27, 2011.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/09/2010, and the submissions filed on 10/25/2010, have been entered.

The Declaration Pursuant to 37 CFR 1.131 filed 10/25/2010

2. The Declaration filed on 10/25/2010 under 37 CFR 1.131 is sufficient to overcome the Parr et al (2003) reference applied under 35 USC 102 and 35 USC 103 as set forth on pages 13-16 of the Office Action of 07/22/2010.

The Declaration Pursuant to 37 CFR 1.132 filed 10/25/2010

3. The Declaration under 37 CFR 1.132 filed 10/25/2010 is sufficient to overcome the rejection of claims under 35 USC 112 1st paragraph for non-enablement of the methods as claimed in so far as they encompass the analysis of Prox-1 protein expression for the diagnostic detection of colon cancer.

The application has been amended as follows:

In the claims:

1. A method of screening colon tissue for colon cancer, said method comprising:

measuring (prospero homeobox protein 1) Prox-1 expression in a biological sample that comprises colon tissue from a human subject; and

screening for colon cancer by:

(a) detecting the presence of an elevated level of Prox-1 expression in said colon tissue in the biological sample that is statistically significantly greater than the level of Prox-1 expression in healthy colon tissue, wherein said presence of the elevated level of Prox-1 expression is indicative of the presence of colon cancer in the colon tissue of the biological sample; or

(b) detecting the absence of an elevated level of Prox-1 expression in said colon tissue in the biological sample that is statistically significantly greater than the level of Prox-1 expression in healthy colon tissue, wherein said absence of the elevated level of Prox-1 expression is indicative of the absence of colon cancer in the colon tissue of the biological sample.

2. (Canceled)

3. The method according to claim 1, further comprising a step, prior to said measuring, of obtaining the biological sample that comprises colon tissue from the human subject.

4. (Canceled)

5. The method according to claim 1, wherein the measuring comprises measuring Prox-1 protein in the colon tissue of the biological sample.

6. The method of claim 5, wherein the measuring comprises contacting the colon tissue of the biological sample with a Prox-1 antibody or antigen-binding fragment thereof.

7. The method of claim 1, wherein the measuring comprises measuring Prox-1 mRNA in the colon tissue of the biological sample.

8. The method of claim 7, wherein the measuring comprises *in situ* hybridization to measure Prox-1 mRNA in the colon tissue of the biological sample.

9. The method of claim 7, wherein the measuring comprises steps of isolating mRNA from the colon tissue of the biological sample and measuring Prox-1 mRNA in the isolated mRNA.

10. The method of claim 1, wherein the measuring comprises quantitative polymerase chain reaction (PCR) to quantify Prox-1 mRNA in the colon tissue in the biological sample relative to Prox-1 mRNA in healthy colon tissue.

11. The method of claim 1, further comprising measuring expression of at least one gene selected from the group consisting of CD44, ectodermal-neural cortex protein

1 (Enc1), and inhibitor of DNA binding 2 (ID2) in the colon tissue of the biological sample.

12. The method of claim 1, further comprising measuring activation of β-catenin/TCF pathway in the colon tissue of the biological sample.

13. The method of claim 12, wherein activation of the β-catenin/TCF pathway is measured by at least one indicator in the colon tissue selected from the group consisting of: mutations in an APC gene; mutations in a β-catenin gene; and nuclear localization of β-catenin.

14. (Canceled)

15. The method of claim 1, wherein the presence of the elevated level of Prox-1 expression is detected in said colon tissue of the biological sample, and wherein the method further comprises administering a composition comprising a Prox-1 inhibitor to the human subject.

16-78. (Canceled)

79. The method of claim 1, wherein the screening step indicates that the human subject has elevated Prox-1 expression in colon tissue and wherein the screening step indicates that the human subject has colon cancer.

80-81. (Canceled)

82. A method of selecting a human subject for therapy with a Prox-1 inhibitor comprising:

(a) screening for colon cancer in the human subject by detecting in a biological sample that comprises colon tissue from the human subject the presence of an elevated

level of Prox-1 expression that is statistically significantly greater than the level of Prox-1 expression in healthy colon tissue, wherein said presence of the elevated level of Prox-1 expression is indicative of the presence of colon cancer in the colon tissue of the biological; and

(b) selecting the human subject identified according to (a) as having the elevated level of Prox-1 for treatment with a Prox-1 inhibitor.

83. (Canceled)

84. The method of claim 82, further comprising a step, prior to said detecting, of obtaining the biological sample from the human subject.

85. The method of claim 82, further comprising administering a Prox-1 inhibitor to the human subject.

86. A method of screening colon tissue for colon cancer, said method comprising:

measuring (prospero homeobox protein 1) Prox-1 expression in a biological sample that comprises colon tissue from a human subject; and

screening for colon cancer by:

(a) detecting the presence of a level of Prox-1 expression in said colon tissue in the biological sample that is statistically similar to the level of Prox-1 expression in colorectal cancer tissue, wherein said level of Prox-1 expression is indicative of the presence of colon cancer in the colon tissue of the biological sample; or

(b) detecting the presence of a level of Prox-1 expression in said colon tissue in the biological sample that is statistically significantly lower than the level of Prox-1

expression in colorectal cancer tissue, wherein said presence of the lower level of Prox-1 expression is indicative of the absence of colon cancer in the colon tissue of the biological sample.

87. (Canceled)

88. The method according to claim 86, wherein the measuring comprises measuring Prox-1 protein in the colon tissue of the biological sample.

89. The method of claim 88, wherein the measuring comprises contacting the colon tissue of the biological sample with a Prox-1 antibody or antigen-binding fragment thereof.

90. The method of claim 86, wherein the measuring comprises measuring Prox-1 mRNA in the colon tissue of the biological sample.

91. The method of claim 90, wherein the measuring comprises *in situ* hybridization to measure Prox-1 mRNA in the colon tissue of the biological sample.

92. The method according to claim 86, wherein the screening indicates that the human subject has colon cancer.

4. The following is an examiner's statement of reasons for allowance:

With the effectiveness of the Declarations pursuant to 37 CFR 1.131 1.132, and the amendments to the claims, as detailed above in this Examiner's Amendment, the claim objections (as set forth on page 4 of the Office Action of 07/22/2010), and the rejections of claims under 35 USC 112 2nd paragraph (as set forth on pages 4-5 of the Office Action of 07/22/2010) and 1st paragraph (as set forth on pages 6-11 of the Office

Action of 07/22/2010), and 35 USC 102 (as set forth on pages 13-14 of the Office Action of 07/22/2010) and 103 (as set forth on pages 14-16 of the Office Action of 07/22/2010) are **WITHDRAWN**. The prior art does not teach or suggest a method wherein overexpression of prox-1 in a colon tissue sample as compared to healthy colon tissue is indicative of the presence of colon cancer in the sample, as is taught in the instant specification.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHEN KAPUSHOC whose telephone number is (571)272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stephen Kapushoc/
Primary Examiner, Art Unit 1634